Annual Report

of the

Diabetes Mellitus

Interagency Coordinating Committee

Fiscal Year 1998

Richard C. Eastman, M.D.

Chairman

Introduction

In accordance with Section 429 of the Public Health Act, the Diabetes Mellitus Interagency Coordinating Committee (DMICC) prepares an annual summary report of its activities as well as other Federal research activities in the field of diabetes. It is submitted to the Secretary, Department of Health and Human Services (DHHS), and the Director of the National Institutes of Health (NIH). This is the annual report of the DMICC for Fiscal Year (FY) 1998.

Legislative Mandate

The DMICC was authorized by Public Law 93-354 and established in fall 1974; subsequent legislation modified some of the charges to the Committee. The legislative authority of the Committee is presented in Appendix A. The charge to the DMICC is to coordinate the research activities of the NIH and other Federal agencies relating to diabetes mellitus and its complications and to contribute to the adequacy and technical soundness of these activities by providing a forum for communication and exchange of information.

The Committee includes representatives from Federal agencies whose programs are relevant to diabetes mellitus and its complications. The chairman, designated by the Director, NIH, is the Director, Division of Diabetes, Endocrinology, and Metabolic Diseases, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). In FY 1998, the DMICC membership included representatives of 21 Federal organizations. A roster of Committee members as of the close of the fiscal year is included as Appendix B.

Activities of the DMICC

The DMICC facilitates cooperation, communication, and collaboration among agencies that conduct or support diabetes-related activities. These activities may range from support for biomedical research to direct provision of health care services. The DMICC provides both a forum for initiating interactions and a mechanism for tracking their progress.

In FY 1998, the DMICC focused its efforts on bringing together members of the diabetes-related scientific community in launching the National Diabetes Education Program (NDEP), a collaboration between the NIDDK and the Centers for Disease Control and Prevention (CDC). It also significantly focused efforts on an approach to eliminating racial and ethnic disparities in diabetes complications by 2010. These efforts are in line with the DHHS initiative to eliminate racial and ethnic disparities in health.

Activities of Member Organizations

Agency for Health Care Policy and Research (AHCPR)

The AHCPR supports a broad range of activities and initiatives in diabetes designed to improve the quality of health care, reduce its costs, and broaden access to essential services that affect policies and practices across the Nation.

Current Activities: (1) The Diabetes Patient Outcomes Research Team (PORT), a multidisciplinary study of type 2 diabetes, was completed. Related publications include an analysis of the effects of insulin therapy on glycemic control and health care use, an analysis of both process and outcomes quality measures in diabetes, and an analysis of the effects of glycemic control on microvascular complications. (2) The ongoing Diabetes Quality Improvement Project (DQIP), based in large part on the work of the PORT, is a collaboration of the National Committee for Quality Assurance, Health Care Financing Administration, American Academy of Family Physicians, Department of Veterans Affairs, American Diabetes Association (ADA), and Foundation for Accountability. The project has developed a common core set of diabetes performance measures that will allow fair comparisons and stimulate quality improvement among health plans and providers. The DQIP measures will be reported in the year 2000 and serve as a baseline for new diabetes projects.

Future Activities: No diabetes-related activities were reported.

Centers for Disease Control and Prevention (CDC) Division of Diabetes Translation

The Division of Diabetes Translation's goal is to reduce the burden of diabetes in the United States by combining support for public health-oriented diabetes control programs nationwide and translation of diabetes research findings into widespread clinical and public health practice.

Current Activities: The Division of Diabetes Translation's diabetes prevention and control program includes (1) supporting diabetes control programs in all 50 states to develop or expand diabetes control efforts; (2) conducting applied translational research focusing on the application of findings from recent randomized control trials in real world settings; (3) supporting the public and private partnership of the NDEP to educate patients, providers, and the public; (4) developing surveillance systems for use at state and local levels, especially for monitoring the diabetes burden among certain racial and ethnic populations; and (5) developing and implementing innovative interventions and prevention strategies for eliminating racial and ethnic health disparities.

In FY 1998, the division significantly strengthened diabetes interventions and prevention strategies to reach disproportionately affected racial and ethnic populations. For example, the division increased special surveillance activities; established the National Diabetes Prevention Center in collaboration with several tribal, federal, medical, and academic partners to address the disproportionate burden of diabetes in American Indians; established the *Diabetes Today* Regional Training Center in Hawaii and a satellite office in Micronesia to provide health professionals and community leaders with the skills needed to mobilize communities and to develop culturally and linguistically appropriate interventions to promote improved diabetes control in Asian and Pacific Island populations; funded several national minority organizations to support NDEP efforts to develop and offer culturally and linguistically appropriate NDEP prevention and control messages through community-based approaches; and collaborated with the University of Illinois at Chicago Research Prevention Center through its Midwest Latino Health Research, Training and Policy Center to replicate and evaluate the culturally specific diabetes empowerment educational program, *Promotora de Salud* (lay health worker)/ *Paso a Paso*.

Future Activities: The division will focus on strengthening the public health system by enhancing the technical assistance provided to the state-based diabetes control programs and increasing the number of comprehensive state-based diabetes control programs as funds become available, increasing special surveillance efforts for high risk populations underrepresented in national surveys, increasing awareness and understanding of the emerging public health problem of type 2 diabetes in children, expanding applied translation research activities in managed care settings, and intensifying the community-based efforts and expanding the educational programs of the NDEP.

Center for Scientific Review (CSR)

The CSR, comprising more than 100 study sections, reviews grant applications in many facets of diabetes research. The Metabolism Study Section reviews most aspects of diabetes research (dedicated mainly to type 2 diabetes and obesity). Other areas of review are the metabolic processes of carbohydrate and lipid pathways in basic (molecular) and clinical settings and the various aspects of beta cell function and regulation of insulin secretion and engineered beta cells. This study section is constantly changed in terms of its consultant membership, in line with the changing trends in diabetes research. Grant applications that address type 1 diabetes are reviewed in several study sections, primarily by the immunological sciences review group.

Current Activities: Three Special Emphasis panels reviewed the NIDDK and other NIH Institutes' request for application (RFA) on Pathogenesis and Complications of Type 2 Diabetes; a total of 140 applications were reviewed in May 1998. Another Special Emphasis panel reviewed 40 applications in the area of glucose sensors.

Future Activities: The CSR will continue to provide peer-review support of grant applications in many areas of type 1 and type 2 diabetes and to contribute to maintaining the high quality of diabetes research supported by NIDDK/NIH within many academic and research institutions across the Nation.

Office of Public Health and Science (OPHS)

No report.

Food and Drug Administration (FDA)

The FDA is charged with approving safe and efficacious agents for public use. This work is especially important for therapeutic agents for the management of diabetes mellitus.

Current Activities: The agency has been carefully monitoring cases of elevated transaminase levels and sporadic cases of irreversible liver failure related to the use of troglitazone. This drug is the prototype of a new class of insulin-sensitizing agents, the thiazolidinediones, that were approved in 1997. The FDA will consider further review of troglitazone's safety profile on the basis of clinical trials data and postmarketing surveillance data. Possible actions include changes in the labeling to limit use and more vigorous monitoring of transaminase levels. Many clinical trials, however, are reporting multiple cardiovascular benefits of troglitazone. The drug decreases hyperinsulinemia by alleviating insulin resistance, which is the hallmark of type 2 diabetes mellitus.

Future Activities: No diabetes-related activities were reported.

Health Care Financing Administration (HCFA)

No report.

Health Resources and Services Administration (HRSA)

HRSA manages a number of health care systems development programs. Although they are not specific to diabetes, they all include elements of diabetes education, prevention, recognition, or treatment as appropriate.

Current Activities: The Bureau of Primary Health Care (BPHC) funds about 730 community-based health center programs for special populations; all clinical programs include appropriate diabetes screening and treatment. (1) The BPHC initiated an evidence-based strategy that includes two HBA1C tests at least 3 months apart, focuses on population-based care to assure that all relevant members of a population receive needed services, and is patient centered, increasing the participation, confidence, and skills of patients to self-manage their diabetes. The strategy aims to decrease the complications and economic burden of diabetes and to improve access to diabetes care for underserved populations. Part of a 6-year project, this initiative involves partnerships with the Institute for Healthcare Improvement, CDC, NIH, ADA, National Committee for Quality Assurance, and National Association of Community Health Centers. (2) The BPHC also supports efforts to discourage foot pathology. The Bureau promotes and manages the Lower Extremity Amputation Prevention (LEAP) program and a Patient Empowerment Program, which trains patients and families to screen for diabetic neuropathy. This program incorporates the Healthy People 2000 goal of reducing amputations by 40 percent. LEAP assists the ADA, Veterans' Administration, and Boehringer-Mannheim/Lilly Alliance Amputation Prevention Program in developing methods and devices for screening and treating diabetic neuropathy.

The Bureau of Health Professions administers several programs supporting health professions education; education in diabetes management is a fundamental aspect of the training of primary care practitioners. Individual projects, based on community needs, may focus on diabetes. For example, the Interdisciplinary Rural Training Program supports a diabetes program in Nebraska for two Native American communities, the Winnebago and the Omaha.

The Maternal and Child Health Bureau (MCHB) administers MCH Block Grants to states to support maternal and child health programs. Information, screening for childhood diabetes, and the development of programs for diabetes care are supported under these grants. MCHB also funds about 800 discretionary grants for Special Projects of Regional and National Significance that do not administer activities specifically targeted to diabetes but do address core elements of community systems of care serving all children with special health care needs. MCHB's Healthy Start Initiative, designed to reduce infant mortality by 50 percent in targeted communities, includes services addressing diabetes in mothers and children. MCHB also promotes diabetes detection and care through school-based and school-linked health programs and through programs that provide primary health care to incarcerated youth.

The Office of Special Programs supports the Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients. In December 1997, HRSA and the DHHS launched the National Organ and Tissue Donation Initiative together with hundreds of public and private organizations, including the ADA, to educate people about the need for more organ donations.

Future Activities: HRSA will continue to support these diabetes-related activities.

National Center for Research Resources (NCRR)

The NCRR develops and supports research technologies and shared resources that are critically important to the research efforts directed at maintaining and improving the health of our Nation's citizens. To facilitate health-related research, the NCRR also supports the development and use of sophisticated instrumentation and technologies, animal models of human disease, and clinical research environments. Programs provide support for the career development of biomedical investigators who address new and emerging biomedical technologies for both patient and veterinary research on diabetes. The current NCRR diabetes research portfolio includes approximately 600 basic and clinical research subprojects.

Current Activities: Highlights of NCRR-related activities include the finding that individuals who carry an allele associated with control of free fatty acids and glucose metabolism are 2.8 times more likely to develop type 2 diabetes, disruption in the trafficking and translocation of the GLUT4 glucose transporter in skeletal muscle has been shown to be a cause of insulin resistance in humans, strategies for islet cell transplantation are being optimized to treat diabetics, and androgen excess during early rhesus gestation adversely affects pancreatic beta cell function in adulthood. In addition, instruments to identify genes responsible for type 2 diabetic nephropathy are being developed, as are gene therapy strategies to maintain glucose homeostasis and minimally invasive in vivo optical and enzyme thermistor glucose sensors. The effect of angiotensin converting enzyme inhibitors on diabetic retinopathy and the genetic component of insulin resistance in Polynesians are being studied.

Future Activities: The General Clinical Research Centers program, in concert with the Juvenile Diabetes Foundation International, has proposed a national network of Juvenile Diabetes Treatment and Diagnostic Centers. Centers of Clinical Research Excellence at Research Centers in Minority Institutions will be established to focus on diabetes in minority populations. Implantable insulin pumps will be optimized. Reliable feedback control devices will be developed to maintain acceptable blood glucose concentrations. The diabetic swine model will be used to explore the treatment of coronary artery disease. Mutant mouse models will continue to be developed to study insulin-dependent diabetes. A recessive mouse mutation that produces adult onset obesity and hyperproinsulinemia will be studied.

National Eye Institute (NEI)

The NEI conducts and supports research, training, health information dissemination, and other programs concerned with blinding eye diseases, visual disorders, mechanisms of visual function, preservation of sight, and the special health problems and requirements of the blind. Diabetes is responsible for the ocular disease diabetic retinopathy, which is the leading cause of blindness in people between the ages of 24 and 70 years.

Current Activities: Highlights of NEI-supported research include (1) the finding that an endothelial nitric oxide synthase-dependent mechanism is the cellular route by which the vascular endothelial growth factor increases retinal endothelial cell permeability. (2) Treatment with d-alpha-tocopherol (vitamin E) prevents diabetes-induced abnormal retinal blood flow in diabetic rats. (3) Studies show that not only vascular cells in the retina but also Müller cells are affected by diabetes. This finding is important for understanding the pathogenesis of diabetic retinal disease. (4) Also, a major effort has been undertaken to identify how many individuals in the Los Angeles Latino community are affected by eye disease, including diabetic retinopathy. Results should assist in setting diabetes health services priorities in the Los Angeles area and the rest of the country.

Future Activities: Conduct and support basic research to gain a greater understanding of the pathogenesis of diabetic retinopathy and develop better methods of preventing, diagnosing, and treating the disease. Continue cooperative efforts with the ADA, through the National Eye Health Education Program, to increase public awareness of diabetes-related eye disease.

National Heart, Lung, and Blood Institute (NHLBI)

The NHLBI supports a comprehensive program spanning basic to clinical research to both understand the ways in which diabetes causes excessive cardiovascular disease and to develop new interventions to prevent or postpone this crippling chronic complication of diabetes.

Current Activities: NHLBI supports observational research in several large diverse populations of men and women with ages ranging from childhood to the elderly using investigator-initiated grants, cooperative agreements, and contracts. Most of these studies have now added a diabetes component to evaluate the effects of diabetes and milder degrees of hyperglycemia on the risk of heart and vascular disease. These studies include multiple minority groups as well as non-Hispanic whites and have enabled NHLBI to quantitate the importance of diabetes as a cardiovascular disease (CVD) risk factor in the different groups. For example, diabetes is a much more important risk factor for CVD in American Indians than it is in non-Hispanic

whites. These studies also enable NHLBI to look at the interaction of other CVD risk factors with diabetes as a cause of CVD.

NHLBI also supports a group of grant-supported laboratory investigations of the relationship between hyperglycemia and related metabolic abnormalities with vascular disease and atherosclerosis. This includes studies of the effects of hyperglycemia as well as inflammation and of insulin and insulin resistance as CVD risk factors. If researchers can increase understanding of the way the metabolic abnormalities of diabetes cause both increased atherosclerosis and cellular dysfunction, it may be possible to design interventions that will block the vascular disease without the need to achieve ideal control of hyperglycemia. An important component of the overall effort is a group of five Program Project grants that have been funded jointly by NHLBI and the Juvenile Diabetes Foundation International. Although primarily focusing on the mechanisms of vascular disease in the laboratory, each also has a clinical component.

Future Activities: NHLBI also supports clinical trials that will provide important evidence on the effectiveness of various interventions designed to reduce heart and large vessel disease in diabetic patients. Chief among these is the ALLHAT study, a clinical trial of antihypertensive therapies that will include almost 15,000 diabetic patients. In addition, ongoing subgroup analyses of the outcomes for diabetic patients are under way in data sets derived from previously completed clinical trials, an approach that may provide additional insight into opportunities to prevent macrovascular disease at very low cost. Finally, planning is under way for a major clinical trial to evaluate different interventions to reduce cardiovascular complications of diabetes.

Research on the causes and treatment of diabetes-associated cardiovascular disease at NHLBI is increasing as it becomes apparent that diabetes and its metabolic abnormalities are among the least understood major risk factors for cardiovascular disease. The NHLBI portfolio of basic research, descriptive clinical studies, and clinical trials should provide new approaches to preventing cardiovascular complications of diabetes.

National Institute of Allergy and Infectious Diseases (NIAID)

No report.

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

The Institute reported that no diabetes-related activities occurred in FY 1998.

National Institute of Child Health and Human Development (NICHD)

The NICHD funds research on preventing type 1 and type 2 diabetes, on behavioral aspects of diabetes mellitus, and on diabetes-related conditions, such as obesity and the polycystic ovarian syndrome. Much of the diabetes research program focuses on gestational and neonatal aspects of diabetes mellitus.

Current Activities: (1) The NICHD cosponsors the Diabetes Prevention Trial, a large, multicenter clinical trial designed to delay or prevent the onset of clinical diabetes in a group of first-degree relatives found to be at high risk by immunological testing. (2) In the Non-Insulin Dependent Diabetes Primary Prevention Trial, designed to prevent or delay the onset of type 2 diabetes, the NICHD supports two centers. The trial evaluates the efficacy of interventions in individuals at increased risk, particularly women who have had gestational diabetes mellitus. (3) The NICHD funds a unique study of the cognitive effects of 60 and 90 minutes of controlled hypoglycemia in diabetic and nondiabetic adolescents between 12 and 18 years of age. (4) To discover the biochemical mechanisms by which diabetes genes function to create susceptibility to diabetes and its complications, the NICHD has developed mouse models to help elucidate the genetic mechanisms that underlie type 2 diabetes. Also, factors involved in the onset of obesity in African American and Caucasian prepubertal girls are being studied, notably energy expenditure, insulin sensitivity, glucose disposal rates, and leptin levels. (5) In studying the in vitro expression of the insulin gene, NICHD-supported investigators have made important progress in determining the tissue-specific expression of the insulin II gene in a rat model.

Future Activities: The NICHD plans to initiate a program with the Juvenile Diabetes Foundation International to cofund grants of mutual interest on type 1 diabetes research; to initiate a 16-site, 5-year prospective international study of hyperglycemia and adverse pregnancy outcomes; and to cosponsor an RFA, "Innovative Approaches to Prevention of Obesity," funding three grants to develop and apply new technologies to ameliorate or prevent obesity and type 2 diabetes in children, adolescents, and young women. The Steering Committee of the Pediatric Pharmacology Research Unit (PPRU) Network will initiate a clinical research study, "Tolerability and Pharmacokinetics of Inhaled Insulin in Children 6–11 Years of Age with Type 1 Diabetes," to be conducted at the PPRU at Yale Medical School.

National Institute of Dental and Craniofacial Research (NIDCR)

The NIDCR supports research on the causes, prevention, diagnosis, and treatment of oral and craniofacial diseases and conditions, including several oral complications associated with diabetes: greater prevalence and severity of periodontal diseases; increased susceptibility to oral mucosal infections; and salivary gland dysfunction and neuropathies resulting in loss or alteration of taste and smell and mucosal sensory perception. The NIDCR also supports research on the effects of oral diseases and conditions on diabetic metabolic control.

Current Activities: (1) In the area of basic science, researchers studied the role of nonenzymatic glycation of extracellular proteins in periodontal diseases, impaired macrophage/monocyte function in diabetics, gingival connective tissue destruction in diabetics, and regulation of beta-cell autoimmunity by Interleukin-10. (2) translational research, researchers studied salivary gland dysfunction in diabetic animals and humans. (3) clinical research, investigators studied diabetes as a risk factor for periodontitis; the association of diabetes, periodontitis, and heart disease; and the treatment of periodontitis in type 2 diabetes in Southwest Native Americans. (4) behavior and health promotion, researchers studied oral health and diabetes, glycemic control in older diabetics, and population-based approaches for oral health care.

Future Activities: The NIDCR will continue to support an Interagency Agreement (Y01) with the Indian Health Service to study treatment of periodontitis in Native Americans with type 2 diabetes and will support a conference in December 1999 on the relationship between oral health and diabetes.

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

The NIDDK is the lead agency of the Federal Government for research efforts to combat diabetes mellitus and its complications. The Division of Diabetes, Endocrinology, and Metabolic Diseases has responsibility for extramural programs related to diabetes research and research training. Additional diabetes-related activities are supported by the Divisions of Intramural Research, Digestive Diseases and Nutrition, and Kidney, Urologic, and Hematologic Diseases.

Current Activities: NIDDK-supported research has made important progress in preventing the devastating health complications of diabetes. The Institute's 10-year, landmark Diabetes Control and Complications Trial (DCCT) showed that very careful management of blood glucose levels dramatically reduces the risk of microvascular complications, such as eye, kidney, and nerve damage, due to diabetes. To facilitate implementation of the DCCT's recommendations, the NIDDK and the CDC developed the NDEP, an outreach effort that aims to improve the treatment and outcomes for people with diabetes, to promote early diagnosis, and, ultimately, to prevent the onset of diabetes. The NIDDK launched the federally sponsored NDEP in June 1998.

In response to FY 1998 congressional report language accompanying the NIH and the NIDDK appropriations, the NIH established a Diabetes Research Working Group (DRWG) on December 1, 1997. This group was charged with developing a comprehensive plan for NIH-funded diabetes research that would recommend future diabetes research initiatives and directions. During 1998, the DRWG held plenary meetings and subcommittee discussions and analyzed the existing NIH diabetes research portfolio. The group evaluated all aspects of the diabetes problem, as well as the state-of-the-science, in an effort to develop a comprehensive plan.

Highlights of other NIDDK diabetes-related activities include research findings that loss of the ability to secrete a growth factor is correlated with the development of type 1 diabetes, that mice lacking a form of tumor necrosis factor are protected from obesity-induced insulin resistance, and that a mutation in transcription of DNA causes maturity onset diabetes of the young. Studies have also suggested that advanced glycation end products and their receptor are involved in the development of accelerated atherosclerosis and new evidence for viral-induced type 1 diabetes in animals.

Future Activities: The NIDDK has taken several steps to guide and facilitate the development of diabetes research initiatives for FY 1999 and FY 2000. The Institute has accelerated and enhanced its efforts by seeking and acting on scientific advice that came out of a special trans-NIH workshop held in September 1997, entitled "Diabetes Mellitus: Challenges and Opportunities," complemented by the strategic planning process of the congressionally established DRWG. Because the Institute is following closely the deliberations of the DRWG, it has been able to jump-start several initiatives before the group publishes its final report and will continue to build on these initiatives in the future.

Within the Institute's ongoing Diabetes Prevention and Treatment Initiative, several activities are being planned, including new clinical trials to prevent the progression of the autoimmune disease process that leads to type 1 diabetes. Another clinical trial will evaluate the role of glycemic control and modulations of insulin resistance in the prevention of macrovascular disease in type 2 diabetes. An initiative for preclinical studies will develop better methods to achieve blood glucose control in diabetic patients.

Two activities will address health disparities in minority populations that are at particular risk for end-stage kidney disease caused by diabetes. One activity will address the cardiovascular disease that is the most important cause of the very high mortality in end-stage kidney disease; risk ratios are as much as fiftyfold greater among minority populations than among the general population. The combination of diabetes and renal disease, specifically, results in very high rates of cardiovascular complications. A multicenter interventional clinical trial will examine the effect of lowering homocysteine levels on cardiovascular risk. A second activity will focus on identifying genes that predispose individuals to develop type 2 diabetes and to the kidney disease of diabetes.

Proposed future activities for the NDEP public awareness campaign include initiating community-based interventions for atrisk populations, incorporating NDEP materials and messages in continuing medical education programs, disseminating science-based guidelines for diabetes care, developing initiatives to promote an integrated approach to care, and increasing awareness about the benefits of glycemic control in the business and labor sectors, including worksite wellness programs.

National Institute of General Medical Sciences (NIGMS)

The NIGMS supports research and research training in the basic biomedical sciences that provide the foundation for a better understanding of fundamental life processes. Some of this work has relevance to understanding and treating diabetes.

Current Activities: (1) The NIGMS supports the Human Genetic Mutant Cell Repository, a collection of more than 6,600 cell lines from individuals with a wide variety of genetic disorders, including diabetes, and from normal individuals. (2) The NIGMS supports grants to develop better statistical methods for mapping and identifying genes and their underlying complex traits, develop mathematical models for studying gene-gene and gene-environment interactions, investigate DNA sequence variation and its evolution, and optimize sampling strategies. (3) The NIGMS supports research on the mechanisms underlying individual variations in drug response that have the potential to affect the treatment of diabetes and its complications.

Future Activities: The NIGMS will continue to support basic research on the underlying mechanisms and principles that are expected to shed light on both normal and disease processes and to lead to the development of new modes of treatment and prevention. Several initiatives are particularly relevant to the pathogenesis and treatment of diabetes; for example, participation in the Trans-NIH Zebrafish Initiative, whose goal is to improve the genomic resources for the zebrafish, a potentially valuable model for diabetes, and cooperation by the Human Genetic Mutant Cell Repository with the National Human Genome Research Institute to acquire a collection of cell lines and DNA from 500 unrelated individuals representative of the diversity of the U.S. population. The latter will help researchers discover DNA polymorphisms, an important step in identifying genes involved in complex genetic disorders such as diabetes.

National Institute of Neurological Disorders and Stroke (NINDS)

The NINDS supports a portfolio of research to study neurological complications of diabetes. More than 60 percent of people with diabetes are affected by neuropathy, and in many patients, symptoms such as pain, numbness, weakness, or even paralysis are serious enough to interfere with daily activities.

Current Activities: (1) A large, ongoing, epidemiologic study of neurological complications of diabetes in the Rochester, Minnesota, area was expanded recently to include a sample from the Mdewakanton Dakota Native American population. Diabetes has been found to be especially prevalent in Native American populations, and this study will be the first to document the extent and progression of neurological complications in such a population. (2) The NINDS participated in the broad RFA "Pathogenesis and Therapy of Complications of Diabetes." Six new grants were funded: three deal with pathogenesis of diabetic neuropathy, two with autonomic neuropathy (a particularly underfunded area), and one with wound healing. (3) More research is being conducted on the other microvascular complications of diabetes (retinopathy and nephropathy), and for this RFA, most of the applications were in these areas.

Future Activities: To promote additional research in neuropathies, the NINDS and NIDDK will issue another RFA soliciting applications dealing with only neurological complications of diabetes.

National Institute of Nursing Research (NINR)

The NINR supports and conducts research and research training on the biological and behavioral processes that underlie promotion of health, amelioration of illness and its sequelae, and effective delivery of care. One purpose of this research, specific to diabetes, is to understand how to promote health-sustaining behavior and to improve quality of life by relieving the effects of disease processes and their progression. Nursing research focuses on how physical and psychological responses

to diabetes symptoms and treatment of the disease affect health throughout the lifespan, and research programs pay particular attention to special populations affected by diabetes.

Current Activities: (1) The NINR funded grants relating to diabetes research, including career development, postdoctoral training, and research. Diabetes-specific topics are autonomic function in youth with insulin-dependent diabetes mellitus, Spanish-language education programs, a study of several Native American tribes, interventions for African American women with diabetes, and interventions for rural dwellers. (2) Staff participated in the DRWG to develop recommendations on diabetes research needs for Congress.

Future Activities: The NINR will continue to support diabetes research on ongoing problems experienced by diabetic individuals and their families and to focus special attention on science areas and populations that have been inadequately studied in the past. Activities will increase research related to diabetes interventions, self-management, quality of life, special populations, basic research, and other initiatives relevant to clinical practice and client outcomes.

National Institute on Aging (NIA)

The NIA supports biomedical and behavioral research leading to improved therapies to prevent diabetes and its complications, as well as the improved quality of life of older patients with diabetes.

Current Activities: (1) Studies are focusing on how known risk factors associated with vasculopathy influence the synthesis and function of advanced glycosylated end products receptors, and how these known risk factors provide a molecular basis for future epidemiology studies and treatment of diabetes- and age-related vascular disease. (2) Because evidence obtained in Fisher 344 rats suggests that glucose intolerance and insulin resistance may be more diet-related than aging-related, further experiments are examining how glucose transport is regulated in skeletal muscle and why a high-fat, refined sugar diet, but not a low-fat, high complex carbohydrate diet, induces insulin resistance. (3) Studies are focusing on the development of interventions (mainly exercise) to reduce abdominal fat and on the factors mediating regional differences in body fat noted in older type 2 patients. (4) The NIA cosponsored the NIDDK study "Diabetes Prevention Program" and collaborated with NIDDK on two new research initiatives on the prevention and treatment of diabetic complications.

Future Activities: Studies will compare the effects of short-term endurance exercise versus reduced caloric intake on insulin sensitivity in older obese men and women, consider exercise interventions for older people with diabetes to explore the mechanisms underlying the exercise-induced benefits in glucose metabolism, examine whole body insulin action and changes in GLUT-4 transporter protein following endurance exercises in young and old subjects, and determine potential defects in signaling pathways that may contribute to the development of insulin resistance in old age. The NIA will continue to cosponsor the NIDDK study "Diabetes Prevention Program" and NIDDK's RFA "Innovative Approaches to Prevention of Obesity."

Veterans Health Administration (VHA)

The VHA is charged with decreasing the prevalence of adverse health outcomes in veterans with diabetes by ensuring that each patient at each facility has access to preventive and treatment programs that meet national standards of care.

Current Activities: (1) The Veterans Administration (VA) was a member of the steering committee of the DQIP. Independent chart review through the VA External Peer Review Program (Headquarters Office of Quality Improvement) paralleled the DQIP measures. (2) An almost complete registry of veterans with diabetes (approximately 500,000 patients from 142 out of 145 facilities) has been created by the VA Health Analysis and Information Group (previously known as the National Center for Cost Containment) by merging pharmacy, laboratory, and outpatient and inpatient ICD9CM codes. (3) In addition to investigator-initiated research, the VA Research Service funded six Diabetes Research Centers in partnership with the Juvenile Diabetes Foundation International/VA Research Partnership (\$3 million annually for 5 years). Also, the VA and Department of Defense (DOD) are collaborating on a \$4 million grant on telemedicine and new technologies for retinopathy screening in collaboration with the Joslin Clinic.

Future Activities: The VHA's Diabetes Clinical Practice Guideline Project will be revised in partnership with the DOD. The VA Health Analysis and Information Group will undertake a comprehensive, collaborative analysis of all diabetes-related lower extremity complications. The VA Research Service will fund the Diabetes Quality Improvement Research Initiative Program to improve the translation of research into practice beginning in FY99.

Interagency Coordinating Committees

Sec. 429. [285c—3] (a) For the purpose of—

- (1) better coordination of the research activities of all the national research institutes relating to diabetes mellitus, digestive diseases, and kidney, urologic, and hematologic diseases; and
- (2) coordinating those aspects of all Federal health programs and activities relating to such diseases to assure the adequacy and technical soundness of such programs and activities and to provide for the full communication and exchange of information necessary to maintain adequate coordination of such programs and activities;

the Secretary shall establish a Diabetes Mellitus Interagency Coordinating Committee, a Digestive Diseases Interagency Coordinating Committee, and a Kidney, Urologic, and Hematologic Diseases Coordinating Committee (hereafter in this section individually referred to as a "Committee").

(b) Each committee shall be composed of the Directors of each of the national research institutes and divisions involved in research with respect to the diseases for which the Committee is established, the Division Director of the Institute for the diseases for which the Committee is established, the Chief Medical Director of the Veterans' Administration, ¹ and the Assistant Secretary of Defense for Health Affairs (or the designees of such officers) and shall include representation from all other Federal departments and agencies whose programs involve health functions or responsibilities relevant to such diseases, as determined by the Secretary. Each Committee shall be chaired by the Director of NIH (or the designee of the Director). Each committee shall meet at the call of the chairman, but not less often than four times a year.

(c) each Committee shall prepare an annual report for—

- (1) the Secretary;
- (2) the Director of NIH; and
- (3) the Advisory Board established under section 430 for the diseases for which the Committee was established, detailing the work of the Committee in carrying out paragraphs (1) and (2) of subsection (a) in the fiscal year for which the report was prepared. Such report shall be submitted not later than 120 days after the end of each fiscal year.

¹ The reference is deemed to be a reference to the Under Secretary for Health of the Department of Veteran Affairs. See section 302(e)(1) of Public Law 102—405 (106) Stat. 1985) and section 10(4) of Public Law 100—527 (102 Stat. 2641).